- Search History will be lost after eight hours of inactivity.
- To combine searches use # before search number, e.g., #2 AND #6.
- Search numbers may not be continuous; all searches are represented.
- Click on query # to add to strategy



| Search | Most Recent Queries | Time | Result |
|---|---|---|---|
| #49 | Search **cyclosporin inhibit and cytosolic calcium** | 17:41:54 | 15 |
| #45 | Search **cyclosporin and mitochondrial calcium and inhibit** | 17:39:12 | 43 |
| #42 | Search **cyclosporin and mitochondrial calcium** | 17:37:30 | 519 |
| #41 | Search **cyclosporin and mitochodrial calcium** | 17:37:00 | 0 |
| #39 | Search **cyclosporin and calcium influx** | 17:36:06 | 120 |
| #38 | Search **cyclosporin and calcium modulator** | 17:30:29 | 20 |
| #37 | Search **cyclosporin and calcium** | 17:29:25 | 2054 |
| #28 | Search **recombinant HCV protein E1** Limits: **Publication Date to 1994/07/29** | 10:54:28 | 12 |
| #25 | Search **yeast and recombinant HCV protein** Limits: **Publication Date to 1994/07/29** | 10:48:19 | 4 |
| #23 | Search **vaccinia vector and recombinant HCV protein** Limits: **Publication Date to 1994/07/29** | 10:46:56 | 2 |
| #21 | Search **vaccinia and HCV envelope protein** Limits: **Publication Date to 1994/07/29** | 10:46:10 | 2 |
| #19 | Search **vector and HCV envelope protein** Limits: **Publication Date to 1994/07/29** | 10:27:07 | 1 |
| #18 | Search **vector and HCV** Limits: **Publication Date to 1994/07/29** | 10:26:54 | 14 |
| #17 | Search **recombinant HCV envelope protein** Limits: **Publication Date to 1994/07/29** | 10:15:21 | 5 |
| #16 | Search **maeten G and HCV envelope protein** Limits: **Publication Date to 1994/07/29** | 10:15:01 | 1 |
| #15 | Search **maeten G and HCV** Limits: **Publication Date to 1994/07/29** | 10:14:45 | 90 |
| #14 | Search **maeten G** Limits: **Publication Date to 1994/07/29** | 10:14:36 | 261176 |
| #13 | Search Field: **All Fields,** Limits: **Publication Date to 1994/07/29** | 10:14:12 | 10153276 |
| #10 | Search **maertens g and hcv and e1** Limits: **Publication Date to 1996/03/11** | 10:07:36 | 3 |
| #9 | Search **maerten G and HCV and E1** Limits: **Publication Date to 1996/03/11** | 10:07:33 | 0 |
| #8 | Search **maerten G and HCV envelope protein E1** Limits: **Publication Date to 1996/03/11** | 10:07:17 | 0 |
| #7 | Search **recombinant HCV envelope protein E1** Field: **All** | 10:06:19 | 1 |

| | | |
|---|---|---|
| **Fields,** Limits: **Publication Date to 1996/03/11** | | |
| #6 Search **recombinant HCV envelope protein E1** Field: **All Fields,** Limits: **Publication Date to 1994/07/29** | 10:05:18 | 1 |
| #4 Search **Koziel M. 1992** | 10:03:43 | 4 |
| #3 Search **Koziel A 1992** | 10:03:29 | 0 |
| #1 Search **Koziel 1993 and HCV** | 10:01:16 | 1 |

Clear History



Jun 27 2005 04:57:20

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| NEWS | 4 | FEB 28 | BABS - Current-awareness alerts (SDIs) available |
| NEWS | 5 | MAR 02 | GBFULL: New full-text patent database on STN |
| NEWS | 6 | MAR 03 | REGISTRY/ZREGISTRY - Sequence annotations enhanced |
| NEWS | 7 | MAR 03 | MEDLINE file segment of TOXCENTER reloaded |
| NEWS | 8 | MAR 22 | KOREAPAT now updated monthly; patent information enhanced |
| NEWS | 9 | MAR 22 | Original IDE display format returns to REGISTRY/ZREGISTRY |
| NEWS | 10 | MAR 22 | PATDPASPC - New patent database available |
| NEWS | 11 | MAR 22 | REGISTRY/ZREGISTRY enhanced with experimental property tags |
| NEWS | 12 | APR 04 | EPFULL enhanced with additional patent information and new fields |
| NEWS | 13 | APR 04 | EMBASE - Database reloaded and enhanced |
| NEWS | 14 | APR 18 | New CAS Information Use Policies available online |
| NEWS | 15 | APR 25 | Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications. |
| NEWS | 16 | APR 28 | Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus |
| NEWS | 17 | MAY 23 | GBFULL enhanced with patent drawing images |
| NEWS | 18 | MAY 23 | REGISTRY has been enhanced with source information from CHEMCATS |
| NEWS | 19 | JUN 06 | The Analysis Edition of STN Express with Discover! (Version 8.0 for Windows) now available |
| NEWS | 20 | JUN 13 | RUSSIAPAT: New full-text patent database on STN |
| NEWS | 21 | JUN 13 | FRFULL enhanced with patent drawing images |
| NEWS | 22 | JUN 27 | MARPAT displays enhanced with expanded G-group definitions and text labels |
| NEWS | 23 | JUL 01 | MEDICONF removed from STN |
| NEWS | 24 | JUL 07 | STN Patent Forums to be held in July 2005 |

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| NEWS EXPRESS | JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005 |
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FILE LAST UPDATED: 11 Jul 2005  (20050711/ED)

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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> HBV
          7924 HBV
            57 HBVS
L1        7940 HBV
                (HBV OR HBVS)

=> cycosporin and L1
             0 CYCOSPORIN
L2           0 CYCOSPORIN AND L1

=> cyclosporin
         14964 CYCLOSPORIN
           372 CYCLOSPORINS
L3       14999 CYCLOSPORIN
                (CYCLOSPORIN OR CYCLOSPORINS)

=> L1 and L3
L4           8 L1 AND L3

=> calcium and L4
        727049 CALCIUM
            32 CALCIUMS
        727052 CALCIUM
                (CALCIUM OR CALCIUMS)
L5           1 CALCIUM AND L4

=> EGTA and L1
         12514 EGTA
             1 EGTAS
         12514 EGTA
                (EGTA OR EGTAS)
L6           1 EGTA AND L1

=> BAPTA and L1
          2813 BAPTA
             1 BAPTAS
```

```
          2814 BAPTA
                 (BAPTA OR BAPTAS)
L7           1 BAPTA AND L1

=> nifedipine and L1
         13397 NIFEDIPINE
L8           1 NIFEDIPINE AND L1

=> nimodipine and l1
          2859 NIMODIPINE
L9           0 NIMODIPINE AND L1

=> felodipine and L1
          1240 FELODIPINE
L10          0 FELODIPINE AND L1

=> isadipine and l1
             0 ISADIPINE
L11          0 ISADIPINE AND L1

=> nicardipine and l1
          3013 NICARDIPINE
             2 NICARDIPINES
          3013 NICARDIPINE
                 (NICARDIPINE OR NICARDIPINES)
L12          0 NICARDIPINE AND L1

=> nosoldipine and l1
             1 NOSOLDIPINE
L13          0 NOSOLDIPINE AND L1

=> nisodipine and l1
             5 NISODIPINE
L14          0 NISODIPINE AND L1

=> benzothiazepine and l1
          1122 BENZOTHIAZEPINE
           541 BENZOTHIAZEPINES
          1300 BENZOTHIAZEPINE
                 (BENZOTHIAZEPINE OR BENZOTHIAZEPINES)
L15          1 BENZOTHIAZEPINE AND L1

=> phenylakylamine and l1
             9 PHENYLAKYLAMINE
             9 PHENYLAKYLAMINES
            17 PHENYLAKYLAMINE
                 (PHENYLAKYLAMINE OR PHENYLAKYLAMINES)
L16          0 PHENYLAKYLAMINE AND L1

=> verapamill and l1
             1 VERAPAMILL
L17          0 VERAPAMILL AND L1

=> diarylaminoprophylamine and l1
             0 DIARYLAMINOPROPHYLAMINE
L18          0 DIARYLAMINOPROPHYLAMINE AND L1

=> bepridili and L1
             0 BEPRIDILI
L19          0 BEPRIDILI AND L1

=> omega-agatoxin and l1
        169079 OMEGA
            12 OMEGAS
        169083 OMEGA
                 (OMEGA OR OMEGAS)
           737 AGATOXIN
            39 AGATOXINS
           752 AGATOXIN
```

```
                (AGATOXIN OR AGATOXINS)
      692 OMEGA-AGATOXIN
                (OMEGA(W)AGATOXIN)
L20         0 OMEGA-AGATOXIN AND L1

=> omega-agatoxin and calcium
   169079 OMEGA
       12 OMEGAS
   169083 OMEGA
                (OMEGA OR OMEGAS)
      737 AGATOXIN
       39 AGATOXINS
      752 AGATOXIN
                (AGATOXIN OR AGATOXINS)
      692 OMEGA-AGATOXIN
                (OMEGA(W)AGATOXIN)
   727049 CALCIUM
       32 CALCIUMS
   727052 CALCIUM
                (CALCIUM OR CALCIUMS)
L21       665 OMEGA-AGATOXIN AND CALCIUM

=> L21 and l1
L22         0 L21 AND L1

=> amilorid and calcium
        8 AMILORID
   727049 CALCIUM
       32 CALCIUMS
   727052 CALCIUM
                (CALCIUM OR CALCIUMS)
L23         1 AMILORID AND CALCIUM

=> L23 and L1
L24         0 L23 AND L1

=> MAPTAM and l1
       30 MAPTAM
L25         0 MAPTAM AND L1

=> calcium (s) inhibitor
   727049 CALCIUM
       32 CALCIUMS
   727052 CALCIUM
                (CALCIUM OR CALCIUMS)
   478437 INHIBITOR
   492791 INHIBITORS
   763351 INHIBITOR
                (INHIBITOR OR INHIBITORS)
L26     11155 CALCIUM (S) INHIBITOR

=> L1 and l26
L27         5 L1 AND L26

=> D L5 IBIB ABS 1-5

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2002:294165  CAPLUS
DOCUMENT NUMBER:          136:304036
TITLE:                    Inhibition of the Src kinase family pathway as a
                          method of treating HBV infection and
                          hepatocellular carcinoma
INVENTOR(S):              Schneider, Robert J.; Klein, Nicola
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 37 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
```

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2002045191 | A1 | 20020418 | US 2001-955006 | 20010917 |
| PRIORITY APPLN. INFO.: | | | US 2000-232892P P | 20000915 |

AB The present invention relates to therapeutic protocols and pharmaceutical compns. designed to target HBx mediated activation of Src kinase, members of the Src tyrosine kinase family and components of the Src kinase family signal transduction pathways for the treatment of **HBV** (hepatitis B virus) infection and related disorders and diseases, such as hepatocellular carcinoma (HCC). The invention further relates to pharmaceutical compns. for the treatment of **HBV** infection targeted to HBx and its essential activities required to sustain **HBV** replication. The invention is based, in part, on the Applicants' discovery that activation of Src kinase signaling cascades play a fundamental role in mammalian hepadnavirus replication. Applicants have demonstrated that HBx mediates activation of the Src family of kinases and that this activation is a critical function provided by HBx for mammalian hepadnavirus replication.

=> D L27 IBIB ABS 1-5

L27 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:639135 CAPLUS
DOCUMENT NUMBER: 142:131910
TITLE: Hepatic cell apoptosis was triggered by HBx accumulation and independent on verapamil
AUTHOR(S): Wang, Haiping; Chen, Xiaoping; Bai, Xiangjun
CORPORATE SOURCE: Department of Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430030, Peop. Rep. China
SOURCE: Journal of Huazhong University of Science and Technology, Medical Sciences (2004), 24(3), 281-283
CODEN: JHUSAW; ISSN: 1672-0733
PUBLISHER: Huazhong University of Science and Technology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To study the roles of HBx and **calcium inhibitor** verapamil in apoptosis of human normal hepatic cells, L02-off, a pTet-off stably integrated human hepatic cell line was established, in which HBx expression was tightly induced by Doxycycline. The effect of different amts. of HBx and verapamil on apoptosis of human normal hepatic cells was detected. The study showed that apoptosis was triggered by accumulation of intracellular HBx, while verapamil had no effects on the apoptotic process. It was concluded that apoptosis mediated by HBx was dose-dependent but calcium-independent.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:567220 CAPLUS
DOCUMENT NUMBER: 141:290790
TITLE: Screening of lymphocyte proteins interacting with hepatitis B virus X antigen by yeast-two hybrid technique
AUTHOR(S): Liang, Yaodong; Cheng, Jun; Li, Qiang; Wang, Lin; Lu, Yinying; Wu, Jun; Cheng, Mingliang
CORPORATE SOURCE: Institute of Infectious Diseases, The 302 Hospital of PLA, Beijing, 100039, Peop. Rep. China
SOURCE: Shijie Huaren Xiaohua Zazhi (2003), 11(12), 1866-1869
CODEN: SHXZF2; ISSN: 1009-3079
PUBLISHER: Shijie Weichangbingxue Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Methods: The hepatitis B virus X antigen (HBxAg) gene was amplified by polymerase chain reaction (PCR) and HBxAg bait plasmid was constructed by using yeast-two hybrid system 3, then transformed into yeast AH109. The

transformed yeast mated with yeast Y187 containing lymphocytes cDNA library plasmid in 2+YPDA medium. Diploid yeast was plated on synthetic dropout nutrient medium (SD/-Trp-Leu-His-Ade) and synthetic dropout nutrient medium (SD/-Trp-Leu-His-Ade) containing X-α-gal for selecting two times and screening. After extracting and sequencing of plasmid from blue colonies, we underwent anal. by bioinformatics. Results: A total of 50 colonies were sequenced. Among them, 20 colonies were eukaryotic translation elongation factor 2, 1 eukaryotic translation elongation factor 1, 2 eukaryotic translation initiation factor 3, 2 protein MTGR1a, 1 myeloid associated differentiation protein, 1 myeloid differentiation primary response protein MYD116, 1 CTCL tumor antigen HD-CL-08, 3 MHC class Ib antigen (HLA-E), 1 leukocyte antigen CD37, 1 aCLL-associated antigen KW-6, 1 lymphocyte function-associated antigen 1, 1 growth arrest and DNA-damage-inducible 34, 2 transcript variant 1, 1 protein phosphatase 1, regulatory **inhibitor** subunit 15 A, 1 cytidine deaminase, 1 macrophage lectin 2 (**calcium** dependent) (HML2), 3 KIAA1949 protein, 1 urokinase-type plasminogen activator receptor, 3 GDP dissociation **inhibitor**, 1 chondroitin 4-sulfotransferase, 1 zinc finger protein, subfamily 1A and a new gene with unknown function. Conclusion: Genes of HBxAg-interacting proteins in lymphocytes are successfully cloned and the results bring some new clues for studying the biol. functions of HBxAg and associated proteins.

L27 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:570687 CAPLUS
DOCUMENT NUMBER: 139:112744
TITLE: Transgenic mouse models for screening for inhibitors of hepatitis B virus
INVENTOR(S): Macejak, Dennis; Lee, Patrice
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of Appl. No. PCT/US02/09187.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 170
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2003140362 | A1 | 20030724 | US 2002-279401 | 20021024 |
| AU 9851819 | A1 | 19980611 | AU 1998-51819 | 19980112 |
| AU 729657 | B2 | 20010208 | | |
| AU 9939188 | A1 | 19990916 | AU 1999-39188 | 19990713 |
| AU 769175 | B2 | 20040115 | AU 2000-56616 | 20000911 |
| WO 2002081494 | A1 | 20021017 | WO 2002-US9187 | 20020326 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 2001-296876P | P | 20010608 |
| US 2001-335059P | P | 20011024 |
| WO 2002-US9187 | A2 | 20020326 |
| AU 1995-26422 | A3 | 19950518 |
| US 1996-623891 | A | 19960325 |
| AU 1996-76662 | A3 | 19961025 |
| US 2001-817879 | A | 20010326 |
| US 2001-877478 | A | 20010608 |
| US 2001-337055P | P | 20011205 |

AB The present invention relates to compds., compns., and methods for the study, diagnosis, and treatment of disease states related to hepatitis B virus (**HBV**) replication and gene expression. **HBV** animal models and methods of use are provided, including methods of

screening for compds. and/or potential therapies directed against **HBV**.

L27 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:526751 CAPLUS
DOCUMENT NUMBER: 139:173263
TITLE: Activation and inhibition of cellular calcium and tyrosine kinase signaling pathways identify targets of the HBx protein involved in hepatitis B virus replication
AUTHOR(S): Bouchard, Michael J.; Puro, Robyn J.; Wang, Lihua; Schneider, Robert J.
CORPORATE SOURCE: Department of Microbiology, New York University School of Medicine, New York, NY, 10016, USA
SOURCE: Journal of Virology (2003), 77(14), 7713-7719
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human hepatitis B virus (**HBV**) HBx protein is a multifunctional protein that activates cellular signaling pathways and is thought to be essential for viral infection. Woodchuck **HBV** mutants that lack HBx are unable to replicate in vivo or are severely impaired. **HBV** replication in HepG2 cells, a human hepatoblastoma cell line, is stimulated 5- to 10-fold by HBx protein. We have utilized the HepG2, HBx-dependent **HBV** replication system to study the effects of activators and **inhibitors** of cytosolic **calcium** and tyrosine kinase signaling pathways on viral replication. By transfecting either a wild-type **HBV** genome or an **HBV** genome that does not express HBx and then treating transfected cells with activators or inhibitors of signaling pathways, we identified compds. that either impair wild-type **HBV** replication or rescue HBx-deficient **HBV** replication. Geldanamycin or herbimycin A, tyrosine kinase inhibitors, blocked **HBV** replication. Derivs. of cyclosporine, i.e., cyclosporine A, cyclosporine H, and SDZ NIM811, which block cytosolic calcium signaling and specifically the mitochondrial permeability transition pore (SDZ NIM811), also impaired **HBV** replication. Treatment of cells with compds. that increase cytosolic calcium levels by a variety of mechanisms rescued replication of an HBx-deficient **HBV** mutant. Transcription of viral RNA and production of viral capsids were only minimally affected by these treatments. These results define a functional signaling circuit for **HBV** replication that includes calcium signaling and activation of cytosolic signaling pathways involving Src kinases, and they suggest that these pathways are stimulated by HBx acting on the mitochondrial transition pore.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:294165 CAPLUS
DOCUMENT NUMBER: 136:304036
TITLE: Inhibition of the Src kinase family pathway as a method of treating **HBV** infection and hepatocellular carcinoma
INVENTOR(S): Schneider, Robert J.; Klein, Nicola
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 37 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2002045191 | A1 | 20020418 | US 2001-955006 | | 20010917 |
| PRIORITY APPLN. INFO.: | | | US 2000-232892P | P | 20000915 |

AB The present invention relates to therapeutic protocols and pharmaceutical

compns. designed to target HBx mediated activation of Src kinase, members of the Src tyrosine kinase family and components of the Src kinase family signal transduction pathways for the treatment of **HBV** (hepatitis B virus) infection and related disorders and diseases, such as hepatocellular carcinoma (HCC). The invention further relates to pharmaceutical compns. for the treatment of **HBV** infection targeted to HBx and its essential activities required to sustain **HBV** replication. The invention is based, in part, on the Applicants' discovery that activation of Src kinase signaling cascades play a fundamental role in mammalian hepadnavirus replication. Applicants have demonstrated that HBx mediates activation of the Src family of kinases and that this activation is a critical function provided by HBx for mammalian hepadnavirus replication.

=> HBx and calcium
823 HBX
727049 CALCIUM
32 CALCIUMS
727052 CALCIUM
(CALCIUM OR CALCIUMS)
L28 21 HBX AND CALCIUM

=> D L28 IBIB ABS 1-21

L28 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:271102 CAPLUS
DOCUMENT NUMBER: 142:422884
TITLE: Inhibitory effect of cyclosporine A on hepatitis B virus replication in vitro and its possible mechanisms
AUTHOR(S): Xia, Wei-Liang; Shen, Yan; Zheng, Shu-Sen
CORPORATE SOURCE: Department of Hepatobiliary Surgery, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, 310003, Peop. Rep. China
SOURCE: Hepatobiliary & Pancreatic Diseases International (2005), 4(1), 18-22
CODEN: HPDIAJ; ISSN: 1499-3872
PUBLISHER: First Affiliated Hospital, Zhejiang University School of Medicine
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. BACKGROUND: Hepatitis B related end-stage liver disease is recently acknowledged as one of the main indications for orthotopic liver transplantation (OLT). However, the high recurrence rate of hepatitis B virus infection following transplantation is regarded as a major factor affecting the long-term survival of transplant recipients especially in China. Cyclosporine A (CsA), which is routinely used to prevent the allograft rejection, is reported to have the inhibitory activity on hepatitis B virus (HBV) replication in vitro. In this paper, we review the inhibitory effect and its possible mechanisms of CsA on HBV replication in vitro. DATA RESOURCES: An English-language literature search was conducted using MEDLINE (1990-2004) on cyclosporine A, hepatitis B virus, mitochondria, **calcium** and other related reports and review articles. RESULTS: Hepatitis B x protein (**HBx**) is essential to HBV replication. The cytosolic **calcium** signaling mediated by mitochondria and the Src kinase pathway were involved during **HBx** activation of HBV replication. CsA inhibits the HBV replication in vitro by its binding to mitochondrial cyclophilin D, then blocking the mitochondria-mediated cytosolic **calcium** signaling. The derivates of CsA also have the HBV replication inhibitory effect in vitro. CONCLUSIONS: By interacting with mitochondria, preventing the release of intramitochondrial **calcium**, and then blocking the cytosolic **calcium** signaling, CsA inhibits the HBV replication in vitro. The derivates of CsA also have this activity.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:248644 CAPLUS

DOCUMENT NUMBER: 142:274057
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 43
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2004241727 | A1 | 20041202 | US 2004-812731 | | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | | 20021009 |
| US 2004241727 | A1 | 20041202 | US 2004-812731 | | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P | 19990106 |
| | | | US 2000-477148 | B1 | 20000104 |
| | | | US 2002-268730 | A2 | 20021009 |
| | | | US 2003-601518 | A2 | 20030620 |
| | | | US 2004-802875 | A2 | 20040312 |
| | | | US 2004-812731 | A | 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L28 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:248643 CAPLUS
DOCUMENT NUMBER: 142:274056
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 43
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2004241727 | A1 | 20041202 | US 2004-812731 | | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | | 20021009 |
| US 2004241727 | A1 | 20041202 | US 2004-812731 | | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P | 19990106 |
| | | | US 2000-477148 | B1 | 20000104 |
| | | | US 2002-268730 | A2 | 20021009 |
| | | | US 2003-601518 | A2 | 20030620 |
| | | | US 2004-802875 | A2 | 20040312 |
| | | | US 2004-812731 | A | 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate

diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L28 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:67524 CAPLUS
DOCUMENT NUMBER: 142:312974
TITLE: **Calcium** ions affect the Hepatitis B virus core assembly
AUTHOR(S): Choi, Yongwook; Park, Sung Gyoo; Yoo, Jun-Hi; Jung, Guhung
CORPORATE SOURCE: School of Biological Sciences, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Virology (2005), 332(1), 454-463
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Previous report showed that cytosolic Ca2+ induced by hepatitis B virus X protein (**HBx**) promotes HBV replication. In this study, in vitro expts. showed that (i) HBV core assembly in vitro was promoted by Ca2+ through the sucrose d. gradient and the anal. ultracentrifuge anal. Also, (ii) transmission electron microscope anal. demonstrated these assembled HBV core particles were the capsids. Ex vivo expts. showed that the treatment of BAPTA-AM and cyclosporine A (CsA) reduced HBV capsids in the transfected HepG2 cells. In addition to that, the treatment of Thapsigargin (TG) increased HBV capsids in the transfected HepG2 cells. Furthermore, we investigated the increased HBV core assembly by **HBx**. The results show that the increased cytosolic **calcium** ions by **HBx** promote the HBV core assembly.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:60754 CAPLUS
Correction of: 2004:1036571
DOCUMENT NUMBER: 142:233342
Correction of: 142:16836
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 43
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2004241727 | A1 | 20041202 | US 2004-812731 | | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | | 20021009 |
| US 2004241727 | A1 | 20041202 | US 2004-812731 | | 20040330 |
| US 2004241727 | A1 | 20041202 | US 2004-812731 | | 20040330 |
| US 2004265869 | A1 | 20041230 | US 2004-812716 | | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P | 19990106 |
| | | | US 2000-477148 | B1 | 20000104 |
| | | | US 2002-268730 | A2 | 20021009 |
| | | | US 2003-601518 | A2 | 20030620 |
| | | | US 2004-802875 | A2 | 20040312 |
| | | | US 2004-812731 | A | 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which

delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L28 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:17963 CAPLUS
DOCUMENT NUMBER: 142:427440
TITLE: Progress of study on biological characteristics of **HBx** protein
AUTHOR(S): Shen, Hui
CORPORATE SOURCE: Second Clinical Medical College, Shanxi Medical University, Taiyuan, 030001, Peop. Rep. China
SOURCE: Shanxi Yike Daxue Xuebao (2004), 35(2), 189-191
CODEN: SDXYF5; ISSN: 1007-6611
PUBLISHER: Shanxi Yike Daxue Xuebao Bianjishi
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review discusses the roles of hepatitis B virus (HBV) X protein ( **HBx**) in the carcinogenesis of HBV with three subdivision headlines: (1) **HBx** and proteasome complex; (2) **HBx** and signal transduction of PI3-K (phosphatidylinositol-3 kinase) and **calcium**; (3) effects of **HBx** on cell migration and invasive phenotypes of tumor.

L28 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:836078 CAPLUS
DOCUMENT NUMBER: 142:33552
TITLE: Nuclear respiratory factor 1 plays an essential role in transcriptional initiation from the hepatitis B virus X gene promoter
AUTHOR(S): Tokusumi, Yumiko; Zhou, Sharleen; Takada, Shinako
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Genes and Development Program of the Graduate School of Biomedical Sciences, University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
SOURCE: Journal of Virology (2004), 78(20), 10856-10864
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The X gene of hepatitis B virus (HBV) is one of the major factors in HBV-induced hepatocarcinogenesis and is essential for the establishment of productive HBV replication in vivo. Recent studies have shown that the X gene product targets mitochondria and induces **calcium** flux, thereby activating Ca+-dependent signal transduction pathways. However, regulatory mechanisms of X gene expression have remained unclear. Previous studies had localized a minimal promoter activity to a 21-bp GC-rich sequence located 130 bp upstream of the X protein coding region and showed that there was a cellular protein bound to this DNA. Interestingly, the 21-bp sequence identified as an X gene minimal promoter does not contain any previously identified core promoter elements, such as a TATA box. To better understand the mechanisms of transcriptional initiation of the X gene, we set out to biochem. purify the binding protein(s) for the 21-bp DNA. We report here the identification of the X gene minimal promoter-binding activity as nuclear respiratory factor 1 (NRF1), a previously known transcription factor that activates the majority of nucleus-encoded mitochondrial genes and various housekeeping genes. Primer extension analyses of the X mRNAs show that mutations at the binding site specifically inactivate transcription from this promoter and that a dominant-neg. NRF1 mutant and short interfering RNAs inhibit transcription from this promoter. Therefore, NRF1 specifically binds the 21-bp minimal promoter and pos. contributes to transcription of the X gene. Simultaneous activation of the X gene and mitochondrial genes by NRF1 may allow the X protein to target mitochondria most efficiently.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:639135 CAPLUS
DOCUMENT NUMBER: 142:131910
TITLE: Hepatic cell apoptosis was triggered by **HBx** accumulation and independent on verapamil
AUTHOR(S): Wang, Haiping; Chen, Xiaoping; Bai, Xiangjun
CORPORATE SOURCE: Department of Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430030, Peop. Rep. China
SOURCE: Journal of Huazhong University of Science and Technology, Medical Sciences (2004), 24(3), 281-283
CODEN: JHUSAW; ISSN: 1672-0733
PUBLISHER: Huazhong University of Science and Technology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To study the roles of **HBx** and **calcium** inhibitor verapamil in apoptosis of human normal hepatic cells, L02-off, a pTet-off stably integrated human hepatic cell line was established, in which **HBx** expression was tightly induced by Doxycycline. The effect of different amts. of **HBx** and verapamil on apoptosis of human normal hepatic cells was detected. The study showed that apoptosis was triggered by accumulation of intracellular **HBx**, while verapamil had no effects on the apoptotic process. It was concluded that apoptosis mediated by **HBx** was dose-dependent but **calcium** -independent.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:567220 CAPLUS
DOCUMENT NUMBER: 141:290790
TITLE: Screening of lymphocyte proteins interacting with hepatitis B virus X antigen by yeast-two hybrid technique
AUTHOR(S): Liang, Yaodong; Cheng, Jun; Li, Qiang; Wang, Lin; Lu, Yinying; Wu, Jun; Cheng, Mingliang
CORPORATE SOURCE: Institute of Infectious Diseases, The 302 Hospital of PLA, Beijing, 100039, Peop. Rep. China
SOURCE: Shijie Huaren Xiaohua Zazhi (2003), 11(12), 1866-1869
CODEN: SHXZF2; ISSN: 1009-3079
PUBLISHER: Shijie Weichangbingxue Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Methods: The hepatitis B virus X antigen (HBxAg) gene was amplified by polymerase chain reaction (PCR) and HBxAg bait plasmid was constructed by using yeast-two hybrid system 3, then transformed into yeast AH109. The transformed yeast mated with yeast Y187 containing lymphocytes cDNA library plasmid in 2+YPDA medium. Diploid yeast was plated on synthetic dropout nutrient medium (SD/-Trp-Leu-His-Ade) and synthetic dropout nutrient medium (SD/-Trp-Leu-His-Ade) containing X-α-gal for selecting two times and screening. After extracting and sequencing of plasmid from blue colonies, we underwent anal. by bioinformatics. Results: A total of 50 colonies were sequenced. Among them, 20 colonies were eukaryotic translation elongation factor 2, 1 eukaryotic translation elongation factor 1, 2 eukaryotic translation initiation factor 3, 2 protein MTGR1a, 1 myeloid associated differentiation protein, 1 myeloid differentiation primary response protein MYD116, 1 CTCL tumor antigen HD-CL-08, 3 MHC class Ib antigen (HLA-E), 1 leukocyte antigen CD37, 1 aCLL-associated antigen KW-6, 1 lymphocyte function-associated antigen 1, 1 growth arrest and DNA-damage-inducible 34, 2 transcript variant 1, 1 protein phosphatase 1, regulatory inhibitor subunit 15 A, 1 cytidine deaminase, 1 macrophage lectin 2 (**calcium** dependent) (HML2), 3 KIAA1949 protein, 1 urokinase-type plasminogen activator receptor, 3 GDP dissociation inhibitor, 1 chondroitin 4-sulfotransferase, 1 zinc finger protein, subfamily 1A and a new gene with unknown function. Conclusion: Genes of HBxAg-interacting proteins in lymphocytes are successfully cloned and the results bring some new clues for studying the biol. functions of HBxAg and associated proteins.

L28 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:760736 CAPLUS
DOCUMENT NUMBER: 139:349012
TITLE: Activation of **calcium** signaling by hepatitis B virus-X protein in liver cells
AUTHOR(S): Oh, Jane C.; Jeong, Deuk-Lim; Kim, In-Kyung; Oh, Sang-Hwan
CORPORATE SOURCE: Department of Biochemistry, College of Medicine, The Catholic University of Korea, Seoul, 137-701, S. Korea
SOURCE: Experimental and Molecular Medicine (2003), 35(4), 301-309
CODEN: EMMEF3; ISSN: 1226-3613
PUBLISHER: Korean Society of Medical Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hepatitis B virus x gene product (**HBx**) is known to be a transactivator of transcriptional elements that regulate the expression of a variety of genes associated with the growth, differentiation, survival and the apoptosis of cells. However, the exact mechanism of the activation and inhibition of cellular events by **HBx** remains uncertain. The present study was designed to measure the effect of **HBx**, on the signal transduction pathways associated with intracellular Ca2+ mobilization following **HBx** transfection in the stable Chang liver cells (CHL-X). Enhanced cell proliferation by **HBx** in CHL-X was confirmed by MTT assay and by the immunodetection of PCNA. The transactivation of AP-1 by **HBx** induced in CHL-X was inhibited by cyclosporin A (CsA), a mitochondrial Ca2+ channel blocker and by BAPTA-AM, a cytosolic Ca2+ blocker. Activation of the SAPK/JNK signaling pathway by **HBx** was evidenced by the increased phosphorylations of c-Jun (Ser63) and of JNK (Thr183/Tyr185). Increased phospho-Erk/Erk and phospho-Raf1/Raf in **HBx**-induced CHL-X indicated that **HBx** might stimulate the MAPK pathway. PI3K activity and cytosolic free Ca2+ levels were elevated in **HBx**-induced CHL-X. These results imply that **HBx** transactivates both JNK and MAPK signal transduction pathways in association with the mobilization of cytosolic Ca2+.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:647468 CAPLUS
DOCUMENT NUMBER: 139:228404
TITLE: Caspase-dependent Alterations of Ca2+ Signaling in the Induction of Apoptosis by Hepatitis B Virus X Protein
AUTHOR(S): Chami, Mounia; Ferrari, Davide; Nicotera, Pierluigi; Paterlini-Brechot, Patrizia; Rizzuto, Rosario
CORPORATE SOURCE: Section of General Pathology and Interdiscipliny Center for the Study of Inflammation, Department of Experimental and Diagnostic Medicine, Ferrara, I-44100, Italy
SOURCE: Journal of Biological Chemistry (2003), 278(34), 31745-31755
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The hepatitis B virus X protein (**HBx**) is a multifunctional protein, acting on different targets (e.g. transcription factors, cytoplasmic kinases, and mitochondrial proteins) and exerting cellular effects as diverse as stimulation of cell proliferation and apoptosis. In its biol. effects, the modulation of cellular Ca2+ signals has been proposed to be involved, but the direct assessment of Ca2+ homeostasis in **HBx**-transfected cells has not been carried out yet. In this work, we have employed for this purpose aequorin-based recombinant probes specifically targeted to intracellular organelles and microdomains. Using these probes, we observed that overexpression of **HBx** enhanced agonist-evoked cytosolic Ca2+ signals in HepG2 and HeLa cells, without affecting either the steady state of endoplasmic reticulum Ca2+ concentration or

the kinetics of Ca2+ release. Rather, caspase-3-dependent cleavage of the plasma membrane Ca2+ ATPase could be demonstrated, and larger rises were detected in the cytoplasmic rim beneath the plasma membrane. In mitochondria, major morphol. (fragmentation and swelling) and functional (reduced Ca2+ uptake) alterations were detected in **HBx** -expressing cells. As to the cellular consequences, we observed that **HBx**-induced apoptosis was markedly reduced when the alterations in Ca2+ signaling (e.g. by loading a Ca2+ chelator or preventing PMCA cleavage) or the downstream effects (e.g. by inhibiting mitochondrial permeability transition) were prevented. Overall, these results indicate that **HBx** perturbs intracellular Ca2+ homeostasis, acting on the extrusion mechanisms, and that this effect plays an important role in the control of **HBx**-related apoptosis.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:526751 CAPLUS

DOCUMENT NUMBER: 139:173263

TITLE: Activation and inhibition of cellular **calcium** and tyrosine kinase signaling pathways identify targets of the **HBx** protein involved in hepatitis B virus replication

AUTHOR(S): Bouchard, Michael J.; Puro, Robyn J.; Wang, Lihua; Schneider, Robert J.

CORPORATE SOURCE: Department of Microbiology, New York University School of Medicine, New York, NY, 10016, USA

SOURCE: Journal of Virology (2003), 77(14), 7713-7719
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human hepatitis B virus (HBV) **HBx** protein is a multifunctional protein that activates cellular signaling pathways and is thought to be essential for viral infection. Woodchuck HBV mutants that lack **HBx** are unable to replicate in vivo or are severely impaired. HBV replication in HepG2 cells, a human hepatoblastoma cell line, is stimulated 5- to 10-fold by **HBx** protein. We have utilized the HepG2, **HBx**-dependent HBV replication system to study the effects of activators and inhibitors of cytosolic **calcium** and tyrosine kinase signaling pathways on viral replication. By transfecting either a wild-type HBV genome or an HBV genome that does not express **HBx** and then treating transfected cells with activators or inhibitors of signaling pathways, we identified compds. that either impair wild-type HBV replication or rescue **HBx**-deficient HBV replication. Geldanamycin or herbimycin A, tyrosine kinase inhibitors, blocked HBV replication. Derivs. of cyclosporine, i.e., cyclosporine A, cyclosporine H, and SDZ NIM811, which block cytosolic **calcium** signaling and specifically the mitochondrial permeability transition pore (SDZ NIM811), also impaired HBV replication. Treatment of cells with compds. that increase cytosolic **calcium** levels by a variety of mechanisms rescued replication of an **HBx**-deficient HBV mutant. Transcription of viral RNA and production of viral capsids were only minimally affected by these treatments. These results define a functional signaling circuit for HBV replication that includes **calcium** signaling and activation of cytosolic signaling pathways involving Src kinases, and they suggest that these pathways are stimulated by **HBx** acting on the mitochondrial transition pore.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:208233 CAPLUS

DOCUMENT NUMBER: 139:33003

TITLE: Regulation of Galβ1, 3GalNAcα2, 3-sialyltransferase by Hepatitis B Virus MHBs/ **HBx** transactivator

AUTHOR(S): Ding, Huiping; Wang, Junqi; Jin, Cheng

CORPORATE SOURCE: State Key Laboratory of Microbial Resources, Institute

of Microbiology, Chinese Academy of Sciences, Beijing, 100080, Peop. Rep. China
SOURCE: Shengwu Gongcheng Xuebao (2002), 18(5), 551-555
CODEN: SGXUED; ISSN: 1000-3061
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Hepatitis B virus MHBst and **HBx** fragments were amplified to construct eukaryotic expression vector pCDNA3.1-MH-Bst and pCDNA3.1-**HBx**. ST3GalI promoter region was obtained by the method of PCR and GFP report plasmid pEGFP-N1-Psial was constructed. PCDNA3.1-MHBst or pCDNA3.1-**HBx** with pEGFP-N1-Psial were transiently co-transfected into QGY-7701 cells using **calcium** phosphate-DNA co-precipitation, resp. The expressions of Psial-directed GFP were analyzed by FAC-Scalibur. It was found that MHBsT/**HBx** could upregulate ST3GalI promoter activity by 35.2% and 43.8%, resp. The regulation of ST3GalI by MHBst and **HBx** trans-activators was reported. It would be helpful to further investigate the relation between hepatitis B virus infection and sialyltransferase expression.

L28 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:715719 CAPLUS
DOCUMENT NUMBER: 137:367569
TITLE: Hepatitis B virus X protein activates the p38 mitogen-activated protein kinase pathway in dedifferentiated hepatocytes
AUTHOR(S): Tarn, Chi; Zou, Lin; Hullinger, Ronald L.; Andrisani, Ourania M.
CORPORATE SOURCE: Department of Basic Medical Sciences, Purdue University, West Lafayette, IN, 47907-1246, USA
SOURCE: Journal of Virology (2002), 76(19), 9763-9772
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hepatitis B virus X protein (pX) is implicated in hepatocarcinogenesis by an unknown mechanism. Employing a cellular model linked to pX-mediated transformation, we investigated the role of the previously reported Stat3 activation by pX in hepatocyte transformation. Our model is composed of a differentiated hepatocyte (AML12) 3pX-1 cell line that undergoes pX-dependent transformation and a dedifferentiated hepatocyte (AML12) 4pX-1 cell line that does not exhibit transformation by pX. We report that pX-dependent Stat3 activation occurs only in non-pX-transforming 4pX-1 cells and conclude that Stat3 activation is not linked to pX-mediated transformation. Maximum Stat3 transactivation requires Ser727 phosphorylation, mediated by mitogenic pathway activation. Employing dominant neg. mutants and inhibitors of mitogenic pathways, we demonstrate that maximum, pX-dependent Stat3 transactivation is inhibited by the p38 mitogen-activated protein kinase (MAPK)-specific inhibitor SB 203580. Using transient-transreporter and in vitro kinase assays, we demonstrate for the first time that pX activates the p38 MAPK pathway only in 4pX-1 cells. PX-mediated Stat3 and p38 MAPK activation is Ca2+ and c-Src dependent, in agreement with the established cellular action of pX. Importantly, pX-dependent activation of p38 MAPK inactivates Cdc25C by phosphorylation of Ser216, thus initiating activation of the G2/M checkpoint, resulting in 4pX-1 cell growth retardation. Interestingly, pX expression in the less differentiated hepatocyte 4pX-1 cells activates signaling pathways known to be active in regenerating hepatocytes. These results suggest that pX expression in the infected liver effects distinct mitogenic pathway activation in less differentiated vs. differentiated hepatocytes.
REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:629912 CAPLUS
DOCUMENT NUMBER: 137:215682
TITLE: The Hepatitis B Virus X Protein Binds to and Activates the NH2-Terminal trans-Activation Domain of Nuclear

Factor of Activated T Cells-1
AUTHOR(S): Carretero, Marta; Gomez-Gonzalo, Marta; Lara-Pezzi, Enrique; Benedicto, Ignacio; Aramburu, Jose; Martinez-Martinez, Sara; Redondo, Juan Miguel; Lopez-Cabrera, Manuel
CORPORATE SOURCE: Unidad de Biologia Molecular, Hospital Universitario de la Princesa, Madrid, 28006, Spain
SOURCE: Virology (2002), 299(2), 288-300
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have previously reported that the hepatitis B virus X protein ( **HBx**) activates nuclear factor of activated T cells (NF-AT), a key regulator of the immune system, by a **calcium**/calcineurin-dependent pathway, involving dephosphorylation and nuclear translocation of this transcription factor. In addition, we showed that **HBx** synergizes with potent **calcium**-mobilizing stimuli to activate NF-AT-dependent transcription, suggesting that addnl. mechanisms might also be operative in the activation of NF-AT by **HBx**. Here we demonstrate that **HBx** activates the NH2-terminal transcription activation domain (TAD) of NF-AT1 by a mechanism involving protein-protein interaction. Targeting of **HBx** to the nucleus did not affect its ability to induce the transcriptional activity of NF-AT1. In contrast, mutations of **HBx** affecting its functional interaction with general transcription factors abrogated the **HBx**-induced activity of NF-AT1. Together, these results indicate that **HBx** may exert its function by acting as a nuclear coactivator of NF-AT1.
REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:294165 CAPLUS
DOCUMENT NUMBER: 136:304036
TITLE: Inhibition of the Src kinase family pathway as a method of treating HBV infection and hepatocellular carcinoma
INVENTOR(S): Schneider, Robert J.; Klein, Nicola
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 37 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2002045191 | A1 | 20020418 | US 2001-955006 | | 20010917 |
| PRIORITY APPLN. INFO.: | | | US 2000-232892P | P | 20000915 |

AB The present invention relates to therapeutic protocols and pharmaceutical compns. designed to target **HBx** mediated activation of Src kinase, members of the Src tyrosine kinase family and components of the Src kinase family signal transduction pathways for the treatment of HBV (hepatitis B virus) infection and related disorders and diseases, such as hepatocellular carcinoma (HCC). The invention further relates to pharmaceutical compns. for the treatment of HBV infection targeted to **HBx** and its essential activities required to sustain HBV replication. The invention is based, in part, on the Applicants' discovery that activation of Src kinase signaling cascades play a fundamental role in mammalian hepadnavirus replication. Applicants have demonstrated that **HBx** mediates activation of the Src family of kinases and that this activation is a critical function provided by **HBx** for mammalian hepadnavirus replication.

L28 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:915911 CAPLUS
DOCUMENT NUMBER: 136:197934
TITLE: **Calcium** signaling by **HBx** protein

in hepatitis B virus DNA replication
AUTHOR(S): Bouchard, Michael J.; Wang, Li-Hua; Schneider, Robert J.
CORPORATE SOURCE: Department of Microbiology, New York University School of Medicine, New York, NY, 10016, USA
SOURCE: Science (Washington, DC, United States) (2001), 294(5550), 2376-2378
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hepatitis B virus (HBV) infects more than 300 million people and is a leading cause of liver cancer and disease. The HBV **HBx** protein is essential for infection; **HBx** activation of Src is important for HBV DNA replication. In our study, **HBx** activated cytosolic **calcium**-dependent proline-rich tyrosine kinase-2 (Pyk2), a Src kinase activator. **HBx** activation of HBV DNA replication was blocked by inhibiting Pyk2 or **calcium** signaling mediated by mitochondrial **calcium** channels, which suggests that **HBx** targets mitochondrial **calcium** regulation. Reagents that increased cytosolic **calcium** substituted for **HBx** protein in HBV DNA replication. Thus, alteration of cytosolic **calcium** was a fundamental requirement for HBV replication and was mediated by **HBx** protein.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:459407 CAPLUS
DOCUMENT NUMBER: 133:175358
TITLE: Hepatitis B virus-related insertional mutagenesis implicates SERCA1 gene in the control of apoptosis
AUTHOR(S): Chami, Mounia; Gozuacik, Devrim; Saigo, Kenichi; Capiod, Thierry; Falson, Pierre; Lecoeur, Herve; Urashima, Tetsuro; Beckmann, Jack; Gougeon, Marie-Lyse; Claret, Michel; Le Maire, Marc; Brechot, Christian; Paterlini-Brechot, Patrizia
CORPORATE SOURCE: U-370 INSERM, Necker Institute, Paris, 75015, Fr.
SOURCE: Oncogene (2000), 19(25), 2877-2886
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have used the Hepatitis B Virus DNA genome as a probe to identify genes clonally mutated in vivo, in human liver cancers. In a tumor, HBV-DNA was found to be integrated into the gene encoding Sarco/Endoplasmic Reticulum **Calcium** ATPase (SERCA), which pumps **calcium**, an important intracellular messenger for cell viability and growth, from the cytosol to the endoplasmic reticulum. The HBV X gene promoter cis-activates chimeric HBV X/SERCA1 transcripts, with splicing of SERCA1 exon 11, encoding C-terminally truncated SERCA1 proteins. Two chimeric HBV X/SERCA1 proteins accumulate in the tumor and form dimers. In vitro analyses have demonstrated that these proteins localize to the ER, determine its **calcium** depletion and induce cell death. We have also shown that these biol. effects are related to expression of the SERCA, rather than of the viral moiety. This report involves for the first time the expression of mutated SERCA proteins in vivo in a tumor cell proliferation and in vitro in the control of cell viability.
REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:351559 CAPLUS
DOCUMENT NUMBER: 133:3713
TITLE: Generation of antibodies using polynucleotide vaccination in avian species
INVENTOR(S): Duan, Lingxun
PATENT ASSIGNEE(S): Genway Biotech, Inc., USA
SOURCE: PCT Int. Appl., 83 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000029444 | A1 | 20000525 | WO 1999-US26843 | 19991112 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2350111 | AA | 20000525 | CA 1999-2350111 | 19991112 |
| BR 9915732 | A | 20010904 | BR 1999-15732 | 19991112 |
| EP 1133523 | A1 | 20010919 | EP 1999-961658 | 19991112 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002532066 | T2 | 20021002 | JP 2000-582429 | 19991112 |

PRIORITY APPLN. INFO.: US 1998-108487P P 19981116
WO 1999-US26843 W 19991112

AB The present invention relates to a process for producing antibodies to an antigen in an avian species using polynucleotide vaccination. The present invention also relates to a process for determining the proteomics profile of a set of pre-selected DNA sequences isolated from a bio-sample, preferably the proteomics profile of a human cDNA library. The present invention further relates to a process for identifying physiol. distinguishable markers associated with a physiol. abnormal bio-sample.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:543455 CAPLUS
DOCUMENT NUMBER: 127:149994
TITLE: Vinyl chloride resin-based coextruded decorative materials for building exteriors and their manufacture
INVENTOR(S): Hiratsuka, Yuji; Kadono, Masaki; Wazumi, Masahiro
PATENT ASSIGNEE(S): Kanegafuchi Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 09174735 | A2 | 19970708 | JP 1995-336393 | 19951225 |

PRIORITY APPLN. INFO.: JP 1995-336393 19951225

AB The decorative materials (sp. gr. 0.3-0.8 g/cc) with good weather resistance and matte appearance are derived by coextrusion of an acrylic resin containing delustering agent (e.g., crosslinked PMMA) and a low-foaming vinyl chloride resin composition that the acrylic layer accounts for 0.1-1 mm thickness.

L28 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:652205 CAPLUS
DOCUMENT NUMBER: 125:282231
TITLE: Prediction of substitutional behavior of ternary elements in B2-type NiTi, CoTi, FeTi and NiAl
AUTHOR(S): Hosoda, Hideki; Kamio, Akihiko; Suzuki, Tomoo; Mishima, Yoshinao
CORPORATE SOURCE: Dep. Meallurgical Eng., Tokyo Inst. Tech., Tokyo, 152, Japan

SOURCE: Nippon Kinzoku Gakkaishi (1996), 60(9), 793-801
CODEN: NIKGAV; ISSN: 0021-4876
PUBLISHER: Nippon Kinzoku Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB A method is proposed for predicting the substitution behavior of ternary elements (X) in B2-type intermetallic compds. (AB) having substitutional (antistructure) defects at off-stoichiometric compns. Calcns. are carried out using the pseudo-ground state anal. based on the nearest-neighbor, pair-approximation The results revealed that the site preference of X can be determined by both heat of formation and alloy concentration: X occupies A sites only in case of Δ **HBX**<ΔHAB+ΔHAX (ΔHAB stands for the heat of formation between A and B), X occupies B sites only in case of ΔHAX<ΔHAB+Δ **HBX**, and in cased, X occupies both or either A and/or B sites unfilled by constituent elements depending on alloy concentration It is shown that: in NiTi, CoTi, and FeTi, most 3A- and 4A-group elements occupy Ti sites only, and most 8A-, 4B- and 5B-group elements occupy Ni, Co, and Fe sites only; while in NiAl, Co, Rh etc. occupy Ni sites only, and Si occupy Al sites only. These results are in good agreement with available data in the literature.